Paper No. 20

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte HERVE BAZIN and DOMINIQUE LATINNE

Appeal No. 2001-1746
Application No. 09/056,072

ON BRIEF

Before WINTERS, SCHEINER, and ADAMS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 30-44, which are all the claims pending in the application.

Claims 30 and 38 are illustrative of the subject matter on appeal and are reproduced below:

30. An antibody which binds to the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB 11423.

38. A composition, comprising:
a) an antibody which binds to the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB 11423; and

b) a pharmaceutically acceptable carrier, wherein said antibody is present in said composition in an amount effective to inhibit a T-cell mediated immune response.

The references relied upon by the examiner are:

Faustman	5,283,058	Feb. 1, 1994
Queen et al. (Queen)	5,530,101	Jun. 25, 1996
Newman et al. (Newman)	5,658,570	Aug. 19, 1997
Bazin et al. (Bazin I)	5,730,979	Mar. 24, 1998
Bazin et al. (Bazin II)	5,951,983	Sep. 14, 1999

Xia et al. (Xia), "Rat Monoclonal Antibodies Specific for Human T Lymphocytes," in Rat Hybridomas and Rat Monoclonal Antibodies, pp. 309-22 (Bazin ed. 1990)

Bromberg at al. (Bromberg), "Anti-CD2 Monoclonal Antibodies After Cell-mediated Immunity in Vivo," Transplant., Vol. 51, pp. 219-25 (1991)

Gückel et al. (Gückel), "Anti-CD2 Antibodies Induce T Cell Unresponsiveness In Vivo," J. Exp. Med., Vol. 174, pp 957-67 (1991)

Chavin et al. (Chavin), "Prolongation of Allograft and Xenograft Survival in Mice by Anti-CD2 Monoclonal Antibodies," Transplant., Vol. 54, No. 2, pp. 286-91 (1992)

Hafler et al. (Hafler), "Anti-CD4 and Anti-CD2 Monoclonal Antibody Infusions in Subjects with Multiple Sclerosis," J. Immunol., Vol. 141, pp131-38 (1998)

GROUNDS OF REJECTION

I. Claims 30-32, 35-40, and 43 stand rejected under 35 U.S.C. § 102(b) as anticipated by Xia.

II. Claims 30-43 stand rejected under 35 U.S.C. § 103 as being unpatentable over Xia in view of either Queen or Newman, further in view of any one of Gückel, Bromberg, Hafler, Chavin, or Faustman.

III. Claims 30-44 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 18-19 of Bazin I.

IV. Claims 30-43 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of Bazin II.

CLAIM GROUPING

According to appellants' Brief (page 4), "[t]he rejected claims do not stand or fall together, for reasons which will be explained hereinbelow." Claim 38, however, is the only claim separately argued in appellants' Brief. See Brief, page 8 ("the cited prior art does not render obvious to one of ordinary skill in the art the combination of the claimed antibody and an acceptable pharmaceutical carrier, as defined in [c]laim 38..."). As set forth in 37 CFR § 1.192(c)(7) (1999), emphasis added, claims stand or fall together "unless a statement is included that the claims of the group do not stand or fall together and, in the in the argument under paragraph (c)(8) of this section, appellant explains why the claims of the group are believed to be separately patentable."

Therefore, we interpret appellants' statement to mean for: rejection I, claims 31-32, 35-37 stand or fall together with claim 30, and claims 39, 40, and 43 stand or fall together with claim 38; rejection II, claims 31-37 stand or fall together with claim 30, and claims 39-43 stand or fall together with claim 38; rejection III, claims 31-37 stand or fall together with claim 30; and claims 39-44 stand or fall together with claim 38; and rejection IV, claims 31-37 stand or fall together with claim 30; and claims 39-43 stand or fall together with claim 38.

Accordingly, we limit our discussion to representative claims 30 and 38. The remaining claims on appeal will stand or fall together with claims 30 and 38 as set forth above.

DISCUSSION

THE REJECTION UNDER 35 U.S.C. § 102(b):

Anticipation under 35 U.S.C. § 102 requires that a single prior art reference disclose each and every limitation of the claimed invention. Electro Med. Sys. SA v. Cooper Life Sci., 34 F.3d 1048, 1052, 32 USPQ2d 1017, 1019 (Fed. Cir. 1994).

According to the examiner (Answer, page 3), Xia "teach the LO-CD2a-specificity, including hybridomas and methods of making said antibodies and hybridomas of the instant invention." In addition, the examiner argues (id.),

> [a]lthough the reference is silent about a pharmaceutically acceptable carrier pre se, the storage and use of the LO-CD2a antibody in pharmaceutically acceptable carriers such as PBS was well known, practiced and immediately envisaged at the time the invention was made in the art. In addition, the intended use or amount to elicit alloantigen specific hyporesponsiveness would have been met by the reference as such claimed amounts encompass a broad range as the amount of antibody to elicit said immunosuppression would depend on the nature of the system being analyzed or tested.

Claim 30:

Claim 30 is drawn to an antibody that binds to the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB 11423. According to appellants' specification (page 12), "a cell line which produces LO-CD2a, was deposited on July 28, 1993, at the American Type Culture Collection ... and was given the ATCC accession number ATCC HB 11423." Although Xia refers to antibody LO-CD2-act, appellants' disclose (specification, page 23), LO-CD2a is a rat (IgG2b-kappa) anti-CD2 monoclonal

antibody produced and characterized in our laboratory as indicated..." in Xia.[1] Appellants' Brief (bridging sentence, pages 6-7) also confirms that Xia teaches LO-CD2a, "[a]lthough Xia at [p]age 320 indicates that the LO-CD2a antibody binds to an epitope which is different from other antibodies referred to on [p]age 320, Xia does not identify the epitope to which LO-CD2a binds."

According to appellants' (Answer, page 7), "[b]ecause Xia does not define the epitope, Xia does not make LO-CD2a available to one skilled in the art, and one skilled in the art would not have sufficient information to determine whether or not a produced antibody bound to the same epitope as LO-CD2a." As we understand this argument, because Xia does not define the epitope that the LO-CD2a antibody binds, a person of ordinary skill in the art would not have been able to produce an antibody capable of binding the same epitope. We are not persuaded by this argument, because as appellants affirm (Brief, bridging sentence, pages 6-7), Xia teaches the LO-CD2a antibody. While appellants suggest that the LO-CD2a antibody was not available (See e.g., Brief, pages 5-6, and Bierer declaration paragraph 4), appellants have not made an affirmative statement on this record that Xia is not an enabling reference because the LO-CD2a antibody as described by Xia was not made available to the public.

Accordingly, since appellants' admit that Xia teaches the LO-CD2a antibody which, as disclosed in appellants' specification, binds to the same epitope on human lymphocytes as the antibody produced by the cell line

[1] Accordingly, to minimize confusion, we will refer to LO-CD2-act as LO-CD2a for the remainder of our discussion.

deposited as ATCC HB 11423, we agree with the examiner that Xia teaches an antibody which binds to the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB 11423.

In addition, we are not persuaded by appellants argument that the method taught by Xia will not lead to an antibody that binds the same epitope as the antibody produced by the cell line deposited as ATCC HB 11423. According to appellants (Brief, page 5), "[t]he characteristics disclosed by Xia are characteristics common to CD2 antibodies as a class ... [and] do not indicate whether or not an antibody binds to the same epitope as the deposited antibody in that such characteristics are those generally possessed by CD2 antibodies." According to Bierer (declaration, paragraph page 4):

> [T]he Third International Workshop and Conference on Human Leukocyte Differentiation Antigens in Oxford, September 21-26, 1986 ([p]. 149), [(Workshop)]reported several CD2 antibodies which did not react with CEM cells, and did react with MOLT4 cells, HPB-ALL cells and Jurkat cells, whereby the reactivity pattern of Table 4 is not unique to LO-CD2.

We note that appellants fail to rebut the examiner's argument (Answer, page 9) that the antibodies described in the Workshop "do not have the same or identical characteristic profiles" as the LO-CD2a antibody. Nevertheless, the issue is not whether other antibodies are known which exhibit the same reactivity pattern as LO-CD2, there may be. Instead, the issue is whether the examiner met his burden of demonstrating that the Xia teaches an antibody that binds the same epitope as an antibody produced by the cell line deposited as ATCC HB 11423. As discussed above, appellants' admit that Xia teach the LO-CD2a

antibody which was subsequently deposited as ATCC HB 11423. We recognize Bierer's (declaration, paragraph 16) that other antibodies are known which bind CD2 and have a similar reactivity with T cell lines as is set forth in Table 4 of Xia. In our opinion, however, Xia does more than simply identify which cell lines LO-CD2a binds. Xia teaches the methodology for producing hybridomas and antibodies. Xia, pages 310-11. Xia teaches (pages 312-15) the reactivity pattern of LO-CD2a with normal cells and leukemic cells. In this regard, Xia teaches (bridging sentence, pages 312-13), "LO-CD2-a[ ] was less expressed on normal resting T lymphocytes than after their activation by PHA ... [suggesting] [t]his MAb might define an antigen associated with T lymphocyte activation." Xia teach (page 315) that LO-CD2a "precipitated an antigen with molecular weight of 46 kDa from HPB-ALL cells as well as from PHA-activated lymphocytes...." With regard to the CD2 epitope recognized by LO-CD2a, Xia teach (page 316):

> The molecule of 45 to 50 kDa defined by CD2 MAbs bears at least three epitopes. The first two epitopes are present on all T lymphocytes, but only one of them ($T11_1$) functions as an SRBC receptor. The third epitope is hidden on resting T lymphocytes, but appears fully expressed after activation. MAbs directed against these different epitopes can be distinguished by their inhibition of resetting with SRBC or AET-SRBC. ... MAb LO-CD2-a[ ] blocked the resetting of normal PBL with untreated SRBC, but had only a slight effect on resetting of normal PBL with AET-treated SRBC and no effect on rosetting of activated PBL with either AET-treated or untreated SRBC.

Xia also functionally characterize the LO-CD2a antibody (page 318),

> MAb LO-CD2-a[ ] had no effect on PHA-induced proliferation. It lowered the proliferation induced by ConA and PWM (about 50%) and very strongly depressed the antigen-induced proliferation of

> lymphocytes in the case of TT and MLR (85% inhibition). Moreover, activation of lymphocytes through the antigen receptor complex, induced by OKT3, was also strongly inhibited by LO-CD2-a[ ]. We further found that if LO-CD2-a[ ] was present during activation of PBL by OKT3, the interleukin-2 (IL-2) receptor expression was reduced from 63 to 36% (data not shown_. Furthermore, when LO-CD2-a[ ] was added even 3 d after initiation of mixed lymphocyte culture, the inhibition of proliferation remained around 80%, indicating that LO-CD2-a[ ] exerts its effect at a late stage in the process of lymphocyte activation.

We recognize Bierer's statement (declaration, paragraph 14), "the LO-CD2a antibody is not statistically different from a known CD2 antibody; OKT 11." However, in contrast to Bierer's statement, the examiner finds (Answer, page 8) in contrast to OKT11, LO-CD2a "always show a weaker reaction with T lymphocytes than T11 and that LO-CD2 did not react with [the] T cell line CEM, while OKT11 did." See also, Xia, page 320, last line, first full paragraph; and Table 4.

As a whole, we are not persuaded by either appellants' Brief, or the Bierer declaration. While the Brief relies heavily on the Bierer declaration, Bierer discusses Xia's tables individually, and fails to address the significance of the data when viewed as a whole. As the examiner explains (Answer, page 9), "it is the totality of the reactivity patterns and functional characteristics clearly disclosed in Xia et al. that serves to distinguish the LO-CD2[a] antibody specificity over the prior art and not just binding to one cell line or even a few binding characteristics.

As a final note, we disagree with appellants' argument (Brief, page 5) that if "one skilled in the art could not produce the deposited antibody, [sic, antibody

produced by the deposited cell line], one skilled in the art also would not be enabled by Xia to produce an antibody which binds to the same epitope" as the antibody produced by the deposited antibody.[2]

Claim 30 on appeal is drawn to any antibody (a genus of antibodies) that binds to the same epitope as the [LO-CD2a] antibody produced by the cell line deposited as ATCC HB 11423. While it may be true that a person of ordinary skill in the art could not reasonably expect to produce an antibody (a species) that is exactly the same, both chemically and structurally, as an antibody produced by a specific deposited cell line, the antibody (genus) claimed is not so limited in terms of chemistry or structure. Thus, any antibody that is capable of binding the same epitope as the LO-CD2a antibody produced by the cell line deposited as ATCC HB 11423 meets the limitations of claim 30. Cf. In re Argoudelis, 434 F.2d 1390, 168 USPQ 99 (CCPA 1970). The claims under review in Argoudelis were directed to new antibiotic compounds produced by a microorganism. It was conceded that the claimed antibiotic compounds could only be made if one had access to the microorganism starting material. Argoudelis, at 1392, 168 USPQ at 100-101. However, as observed by the Argoudelis court, one "cannot sufficiently disclose by written word how to obtain the microorganism starting material from nature." Argoudelis, at 1392, 168

[2] We note the examiner's discussion (Answer, page 6), of the 5,730,979 and 5,817,311 patents, which reference the antibody produced by cell line deposited as ATCC HB 11423). To the extent that the examiner has attempted to explain the basis for the allowance of the patents we remind the examiner that according to MPEP § 1701, PTO employees are not to discuss questions of validity or invalidity of issued U.S. Patents with persons outside the PTO.

USPQ at 101-102. As the court in Argoudelis, at 1392, 168 USPQ at 102 explained:

> [A] unique aspect of using microorganisms as starting materials is that a sufficient description of how to obtain the microorganism from nature cannot be given. Such a description could only detail an experimental screening program similar to the screening programs followed in discovering the microorganism in the first instance. If the microorganism involved were of very common occurrence, it might be found in a relatively short time, but if it were not of common occurrence, it might not be found for a very long time, if found at all. The microorganism involved here, of course, was not known and available to the workers in the art since it was newly discovered by appellants.

On this record, claim 30 is drawn to any antibody (a genus) that binds the same epitope as the LO-CD2a antibody produced by the cell line deposited as ATCC HB 11423. As discussed above, Xia teach the LO-CD2a antibody and in the alternative teach a method of producing antibodies, and hybridomas producing antibodies, that bind the same epitope as the LO-CD2a antibody produced by the cell line deposited as ATCC HB 11423.

Accordingly, we affirm the rejection of claim 30 under 35 U.S.C. § 102(b) as anticipated by Xia. As set forth supra, claims 31, 32 and 35-37 fall together with claim 30.

Claim 38:

Claim 38, however, stands on a different footing. According to the examiner (Answer, page 3), "[a]lthough the reference is silent about a pharmaceutically acceptable carrier per se, the storage and use of the LO-CD2a antibody in pharmaceutically acceptable carriers such as PBS was well known, practiced and immediately envisaged at the time the invention was made in the

art." The examiner offers no objective evidence to support this conclusion. Cf. In re Lee, 277 F.3d 1338, 1343-1344, 61 USPQ2d 1430, 1433-1434 (Fed. Cir. 2002). Because the examiner failed to provide a sufficient evidentiary basis to sustain a rejection under 35 U.S.C. § 102(b) we are compelled to reverse the rejection of claim 38 under 35 U.S.C. § 102(b) as anticipated by Xia. As set forth supra, claims 39, 40 and 43 stand together with claim 38.

THE REJECTION UNDER 35 U.S.C. § 103:

The examiner relies on Xia as discussed above. Answer, page 3. The examiner finds (id.), however, that Xia does not teach chimeric or humanized antibodies. To make up for the deficiencies of Xia, the examiner relies on Queen and Newman in the alternative. Id. Since the examiner treats the references as cumulative we focus our attention on Queen. According to the examiner (id.), Queen teach "the art-known procedures at the time the invention was made to produce chimeric antibodies starting from hybridoma and antibody producing cells...." In addition, the examiner relies on Gückel, Bromberg, Hafler, Chavin and Faustman to teach therapeutic uses of anti-CD2 antibodies.

According to the examiner (Answer, page 5), "[i]t would have [been] prima facie [sic] obvious to one of ordinary skill in the art at the time the claimed invention was made to generate CD2-specific antibodies including the LO-CD2-specific antibodies to characterize the CD2 specificity and to target said specificity for various biological, diagnostic and therapeutic modalities."

Appellants fail to address any of the secondary or tertiary references relied upon by the examiner. Instead, appellants rely on Thurlow[3] and Giorgi[4]. According to appellants (Brief, page 7), Thurlow "reports that an attempt to use a CD2 monoclonal antibody in a human was not successful[, and Giorgi] reports that another CD2 antibody was not successful in primate studies." In addition, appellants note (Brief, page 7) that pages 40-43 of their specification provides human data of successful treatment.

Claim 30:

As the examiner explains (Answer, page 10), claim 30 does not require the ability to treat humans. Furthermore, the examiner's statement of the rejection is not limited to a therapeutic modality but includes the use of the antibody in various biological and diagnostic modalities. According to Queen (column 20, lines 23-33), humanized antibodies are useful for diagnostic purposes.

For the foregoing reasons, we are not persuaded by appellants' reliance on Thurlow, Giorgi or their specification's evidence of successful human treatment. This evidence simply is not commensurate in scope with the claimed invention. We remind appellants, that in order to establish unexpected results for a claimed invention, objective evidence of non-obviousness must be commensurate in scope with the claims that the evidence is offered to support. In

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[3] Thurlow et al. (Thurlow), "A Monoclonal Anti-Pan-T-Cell Antibody," Transplant., Vol. 35, pp 293-97 (1983).
[4] Giorgi et al. (Giorgi), "Immunosuppressive Effect and Immunogenicity of OKT11A Monoclonal Antibody in Monkey Allograft Recipients," Transplant. Pro., Vol. 36, pp. 293-97 (1983).

re Greenfield, 571 F.2d 1185, 1189, 197 USPQ 227, 230 (CCPA 1978); In re Lindner, 59 CCPA 920, 923, 457 F.2d 506, 508, 173 USPQ 356, 358 (1972); In re Tiffin, 58 CCPA 1420, 1421, 448 F.2d 791, 792, 171 USPQ 294 (1971).

Accordingly, we affirm the rejection of claim 30 under 35 U.S.C. § 103 as being unpatentable over Xia in view of either Queen or Newman, further in view of any one of Gückel, Bromberg, Hafler, Chavin, or Faustman. As set forth supra, claims 31-37 fall together with claim 30.

Claim 38:

Once again, claim 38 stands on a different footing. According to the examiner (Answer, page 10), "the intended use or amount to elicit alloantigen specific hyporesponsiveness was met by the prior art as such claimed functional properties encompass a broad range of activities and a broad range of antibody amounts to elicit immunosuppression depending on the nature of the system being analyzed or tested."

The examiner, however, offers no objective evidence to support this conclusion. Furthermore, notwithstanding the examiner's lack of objective evidence, the examiner fails to establish a nexus between the antibody taught by Xia and any amount capable of eliciting immunosuppression despite the nature of the system being analyzed or tested. Because the examiner failed to provide a sufficient evidentiary basis to sustain a rejection under 35 U.S.C. § 103 we are compelled to reverse the rejection of claim 38 under 35 U.S.C. § 103 as being unpatentable over Xia in view of either Queen or Newman, further in view of any

one of Gückel, Bromberg, Hafler, Chavin, or Faustman. As set forth supra, claims 31-37 fall together with claim 30.

OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTIONS

Bazin I:

Claims 30-44 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 18-19 of Bazin I. Answer, page 6. Appellants' Brief fails to respond to this ground of rejection. Accordingly, we summarily affirm the rejection of claims 30 and 38 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 18-19 of Bazin I. As set forth above, claims 31-37 fall together with claim 30, and claims 39-44 fall together with claim 38.

Bazin II:

Claims 30-43 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of Bazin II. Answer, page 5. We note appellants' statement (Brief, page 4), "[a]pplicants will consider the filing of a terminal disclaimer if the other rejections are reversed." We find no other argument regarding this rejection in appellants' Brief. Accordingly, we summarily affirm the rejection of claims 30 and 38 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of Bazin II. As set forth above, claims 31-37 fall together with claim 30, and claims 39-43 fall together with claim 38.

SUMMARY

The rejection of claims 30-32 and 35-37 under 35 U.S.C. § 102(b) as anticipated by Xia is affirmed.

The rejection of claims 38-40 and 43 under 35 U.S.C. § 102(b) as anticipated by Xia is reversed.

The rejection of claims 30-37 under 35 U.S.C. § 103 as being unpatentable over Xia in view of either Queen or Newman, further in view of any one of Gückel, Bromberg, Hafler, Chavin, or Faustman is affirmed.

The rejection of claims 38-43 under 35 U.S.C. § 103 as being unpatentable over Xia in view of either Queen or Newman, further in view of any one of Gückel, Bromberg, Hafler, Chavin, or Faustman is reversed.

The rejection of claims 30-44 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 18-19 of Bazin I is affirmed.

The rejection of claims 30-43 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of Bazin II is affirmed.

AFFIRMED

Sherman D. Winters)
Administrative Patent Judge)
)
)
Toni R. Scheiner) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
)
) INTERFERENCES
Donald E. Adams)
Administrative Patent Judge)

CARELLA BYRNE BAIN GILFILLAN CECCHI
STEWART & OLSTEIN
6 BECKER FARM ROAD
ROSELAND NJ 07068